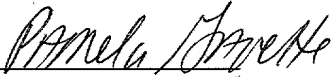


## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Paul J. Godowski et al. Serial No.: Unassigned	Group Art Unit: Unassigned Examiner: Unassigned
Filed: June 6, 2001 For: ErbB4 RECEPTOR-SPECIFIC NEUREGULIN RELATED LIGANDS AND USES THEREFOR	CERTIFICATION UNDER 37 CFR 1.10 EL 809 447 101 US : Express Mail Number June 8, 2001 : Date of Deposit I hereby certify that this correspondence, consisting of Non-Provisional Application Transmittal, Letter and Request to Use Computer-Readable Sequence Listing, copy of Combined Declaration and Power, copy of Extension of Time, postcard, is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner of Patents, Washington, D.C. 20231.  Pamela Gavette

**PRELIMINARY AMENDMENT**

Assistant Commissioner of Patents  
 Washington, D.C. 20231

Sir:

Prior to review of the above-referenced application on the merits, please amend the application as follows:

**In the Specification:**

Please replace the paragraph beginning at page 54, line 22, with the following rewritten paragraph:

-- The simplest and most straightforward immunoadhesin design combines the binding region(s) of the 'adhesin' protein with the hinge and Fc regions of an immunoglobulin heavy chain. Ordinarily, when preparing the NRG3-immunoglobulin chimeras of the present invention, nucleic acid encoding an amino acid sequence of the desired NRG3 polypeptide will be fused at the C-terminus

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encoding portion of the desired sequence to the N-terminus encoding portion of a nucleic acid sequence encoding an immunoglobulin constant domain sequence, however fusion to the N-terminus encoding portion of the desired NRG3 sequence is also possible. Typically, in such fusions the encoded chimeric polypeptide will retain at least functionally active hinge, CH2 and CH3 domains of the constant region of an immunoglobulin heavy chain. Fusions are also made to the C-terminus of the Fc portion of a constant domain, or immediately N-terminal to the CH1 of the heavy chain or the corresponding region of the light chain. The precise site at which the fusion is made is not critical; particular sites are well known and may be selected in order to optimize the biological activity, secretion or binding characteristics of the NRG3-immunoglobulin chimeras.--

**In the Claims:**

Please cancel claims 1-33 and 37-38.

Please amend claim 34 as follows:

34. (Amended) A method of detecting ErbB4 receptor in a sample, the method comprising:

a) contacting a detectably labeled polypeptide with the sample, wherein the polypeptide comprises an EGF-like domain, the EGF-like domain comprising an amino acid sequence having at least 75% amino acid sequence identity to SEQ ID NO:4, and wherein the polypeptide binds to ErbB4 receptor but not ErbB2 receptor or ErbB3 receptor under experimentally comparable conditions; and

b) detecting binding of the polypeptide to a protein in the sample.



Amendments to the specification at page 54 are made to correct inadvertent typographical errors with respect to use of the term "encoding."

No new matter is added by the amendments to the claims. The amendments present the rejected claims in better form for consideration on appeal, should an appeal become necessary. Admission of the amendments and allowance of the claims is respectfully requested.

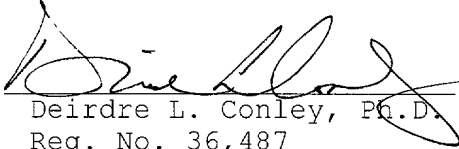
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with Markings to Show Changes Made**".

If the Examiner believes a telephone conference would expedite the prosecution of this application, the Examiner is invited to call the undersigned at the number indicated below.

This response is timely submitted with a transmittal letter. In the unlikely event that these documents are separated from this response, Applicants petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to establish and maintain the pendency of this application.

Respectfully submitted,  
GENENTECH, INC.

Date: June 8, 2001

By:   
Deirdre L. Conley, Ph.D.  
Reg. No. 36,487

1 DNA Way  
So. San Francisco, CA 94080-4990  
Phone: (650) 225-2066  
Fax: (650) 952-9881

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**In the Specification:

Paragraph beginning at line 22 of page 54 has been amended as follows:

The simplest and most straightforward immunoadhesin design combines the binding region(s) of the 'adhesin' protein with the hinge and Fc regions of an immunoglobulin heavy chain. Ordinarily, when preparing the NRG3-immunoglobulin chimeras of the present invention, nucleic acid encoding an amino acid sequence of the desired NRG3 polypeptide will be fused at the C-terminus encoding portion of the desired sequence to the N-terminus encoding portion of a nucleic acid sequence encoding an immunoglobulin constant domain sequence, however fusion to the N-terminus encoding portion of the desired NRG3 sequence is also possible. Typically, in such fusions the encoded chimeric polypeptide will retain at least functionally active hinge, CH2 and CH3 domains of the constant region of an immunoglobulin heavy chain. Fusions are also made to the C-terminus of the Fc portion of a constant domain, or immediately N-terminal to the CH1 of the heavy chain or the corresponding region of the light chain. The precise site at which the fusion is made is not critical; particular sites are well known and may be selected in order to optimize the biological activity, secretion or binding characteristics of the NRG3-immunoglobulin chimeras.

In the Claims:

Please cancel claims 1-33 and 37-38.

Claim 34 has been amended as follows:

34. (Twice Amended) A method of detecting ErbB4 receptor in a sample, the method comprising:

a) contacting a detectably labeled polypeptide with the sample, wherein the polypeptide comprises an EGF-like domain, the EGF-like domain comprising an amino acid sequence having at least 75% amino acid sequence identity to SEQ ID NO:4, and wherein the polypeptide [is capable of binding] binds to ErbB4 receptor but not ErbB2 receptor or ErbB3 receptor under experimentally comparable conditions; and

b) detecting binding of the polypeptide to a protein in the sample.

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### Clean Set of All Pending Claims

34. A method of detecting ErbB4 receptor in a sample, the method comprising:

a) contacting a detectably labeled polypeptide with the sample, wherein the polypeptide comprises an EGF-like domain, the EGF-like domain comprising an amino acid sequence having at least 75% amino acid sequence identity to SEQ ID NO:4, and wherein the polypeptide binds to ErbB4 receptor but not ErbB2 receptor or ErbB3 receptor under experimentally comparable conditions; and

b) detecting binding of the polypeptide to a protein in the sample.

35. The method of claim 34 wherein the sample comprises a cell expressing ErB4 receptor on its surface.

36. The method of claim 35 wherein the sample is a mammalian tissue sample.